Peritoneal dialysis in acute renal failure in canines: A review

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Abstract

Peritoneal dialysis is a technique whereby infusion of dialysis solution into the peritoneal cavity is followed by a variable dwell time and subsequent drainage. During peritoneal dialysis, solutes and fluids are exchanged between the capillary blood and the intraperitoneal fluid through a biologic membrane, the peritoneum. Inadequate renal function leads to disturbance in the removal of the extra fluid and waste products. It removes the waste product and extra fluid from the body in renal failure in small animal practice. Peritoneal dialysis is more accessible, more affordable and easier to administer to the small animal patient. The most common indication for peritoneal dialysis in dogs is acute renal failure (ARF). Peritoneal dialysis is an important therapeutic tool for mitigating clinical signs of uremia and giving the kidneys time to recover in cats with acute kidney injury when conventional therapy is no longer effective.
Key words: Peritoneal dialysis, Acute renal failure, Kidney Disease, Canine.

Introduction

Peritoneal dialysis is a modality of renal replacement therapy that is commonly used in human medicine for treatment of chronic kidney disease and end-stage kidney failure. Peritoneal dialysis uses the peritoneum as a membrane across which fluids and uremic solutes are exchanged. In this process, dialysate is instilled into the peritoneal cavity and, through the process of diffusion and osmosis, water, toxins, electrolytes, and other small molecules, are allowed to equilibrate (Cooper and Labato, 2011).

Peritoneal dialysis uses the peritoneum as a semi permeable layer for dialysis in which excess water, ions and solute in the blood pass through a semi permeable membrane to a sterile solution which is known as dialysate via diffusion, osmosis and filtration. The three-layered peritoneal membrane consists of 1) the mesothelium, a continuous monolayer of flat cells, and their basement membranes; 2) a very compliant interstitium; and 3) the capillary wall, consisting of a continuous layer of mainly non-fenestrated endothelial cells, supported by a basement membrane. The mesothelial layer is considered to be less of a transport barrier to fluid and solutes, including macromolecules, than is the endothelial layer (Clough and Michel, 1988). Solute transport rates are assessed by the rates of their equilibration between the peritoneal capillary blood and dialysate. The ratio of solute concentrations in dialysate and plasma at specific times during the dwell signifies the extent of solute transport. Creatinine and urea clearance rates are the most commonly used indices of dialysis adequacy in clinical settings. Contributions of residual renal clearances are significant in determining the adequacy of dialysis (Flessner *et al.*, 1985).

Mode of action

Hemodialysis is a life-saving medical modality that cleanses the blood using an artificial kidney, called a dialyzer. Hemodialysis uses contact between the patient's blood and the semipermeable membrane of the extracorporeal dialyzer to remove compounds such as blood urea nitrogen, creatinine, electrolytes, minerals, anions, cations, certain drugs and toxins, and excess fluid from the bloodstream. The extracorporeal dialyzer distinguishes hemodialysis from peritoneal dialysis, which uses a patient's peritoneum as the dialysis membrane (Bloom and Labato, 2011).

The capillary endothelial cell membrane is permeable to water through aquaporins (radius of approximately 0.2 to 0.4 nm) (Pannekeet et al., 1996). In addition, small solutes and water are transported through ubiquitous small pores (radius of approximately 0.4 to 0.55 nm). Sparsely populated

large pores (radius of approximately 0.25 nm, perhaps mainly venular) transport macromolecules passively. Diffusion and convection move small molecules through the interstitium with its gel and sol phases, which are restrictive owing to the phenomenon of exclusion. The lymphatic vessels located primarily in the subdiaphragmatic region drain fluid and solutes from the peritoneal cavity through bulk transport. The extent of lymph drainage from the peritoneal cavity is a subject of controversy owing to the lack of a direct method to measure lymph flow (Wade *et al.*, 1956).

Dialysis solution contains electrolytes in physiologic concentrations to facilitate correction of acid-base and electrolyte abnormalities. High concentrations of glucose in the dialysis solution generate ultrafiltration in proportion to the overall osmotic gradient, the reflection coefficients of small solutes relative to the peritoneum, and the peritoneal membrane hydraulic permeability. Removal of solutes such as urea, creatinine, phosphate, and other metabolic end products from the body depends on the development of concentration gradients between blood and intraperitoneal fluid, and the transport is driven by the process of diffusion. The amount of solute removal is a function of the degree of its concentration gradient, the molecular size, membrane permeability and surface area, duration of dialysis, and charge. Ultrafiltration adds a convective component proportionately more important as the molecular size of the solute increases. The peritoneal equilibration test is a clinical tool used to characterize the peritoneal membrane transport properties (Twardowski *et al*., 1987).

Solute transport rates are assessed by the rates of their equilibration between the peritoneal capillary blood and dialysate. The ratio of solute concentrations in dialysate and plasma at specific times during the dwell signifies the extent of solute transport. The fraction of glucose absorbed from the dialysate at specific times can be determined by the ratio of dialysate glucose concentrations at specific times to the initial level in the dialysis solution. Tests are standardized for the following: duration of the preceding exchange before the test; inflow volume; positions during inflow, drain, and dwell; durations of inflow and drain; sampling methods and processing; and laboratory assays (Ahearn and Nolph, 1972).

Creatinine and urea clearance rates are the most commonly used indices of dialysis adequacy in clinical settings. Contributions of residual renal clearances are significant in determining the adequacy of dialysis. The mass-transfer area coefficient (MTAC) represents the clearance rate by diffusion in the absence of ultrafiltration and when the rate of solute accumulation in the dialysis solution is zero (Nolph *et al*., 1979).

Conventional peritoneal dialysis solutions contain glucose, lactate, sodium, potassium, and calcium in differing concentrations. Lactate, bicarbonate or a combination of the two are used to make pH neutral dialysate solutions. Acetate should be avoided because it is associated with loss of ultrafiltration and sclerosing peritonitis. Glucose is the most commonly used osmotic agent and draws fluid across the peritoneal membrane. Newer solutions use alternative osmotic agents including Icodextrin (glucose polymers), for sustained ultrafiltration, or amino acids to address an assumed positive effect on nutritional status (Gokal and Mallick, 1999). These alternative solutions can only be used in a single daily exchange or intermittently and have not been clinically evaluated in veterinary medicine. Dialysate choices include commercial dialysate (e.g., Dianeal) which comes prepared as a 1.25%, 2.5% or 4.5% glucose solution, or home-made alternatives, which include lactated ringers solution (LRS), 0.9% sodium chloride, and 0.45% sodium chloride based on availability as well as the electrolyte status of the patient. Dextrose is added to these solutions to make a 1.25%, 2.5% or 4.5% solution. The concentration of dextrose depends on the hydration status of the patient with higher dextrose concentrations achieving improved ultrafiltration and water removal. A 4.5% solution should only be used when patients are fluid overloaded, and a 1.25% solution is generally adequate in normovolemic patients. Potassium, magnesium, and calcium can be added to the dialysate based on the patient's electrolyte status. The potassium concentration in LRS is 4 mEq/L, this is generally low enough to be used in hyperkalemic patients while still correcting moderate to severe hyperkalemia. If normal saline is used, sodium bicarbonate should be added as a buffer solution at 30–45 mEq/L (Mathews, 2006).

Standard commercial dialysate solutions are designed to remove urea, creatinine, potassium and phosphate from the plasma into the dialysate by the process of diffusion. A variety of dialysate solutions can be used with differing osmolalities on a case by-case basis depending on the ?uid balance of the patient. Fluid and solutes move across the peritoneum by diffusion, ultra?ltration and convection. Urea and potassium diffuse across the peritoneal membrane quickly, whereas creatinine and phosphorus take longer to equilibrate (Zabetakis *et al*., 1993).

During peritoneal dialysis, hyperosmolar

glucose solution generates ultrafiltration by the process of osmosis. Water movement across the peritoneal membrane is proportional to the transmembrane pressure, membrane area, and membrane hydraulic permeability. The transmembrane pressure is the sum of hydrostatic and osmotic pressure differences between the blood in the peritoneal capillary and dialysis solution in the peritoneal cavity (Wolf *et al*., 1992). Net transcapillary ultrafiltration defines net fluid movement from the peritoneal microcirculation into the peritoneal cavity primarily in response to osmotic pressure. Net ultrafiltration would equal the resulting increment in intraperitoneal fluid volume if it were not for peritoneal reabsorption, mostly through the peritoneal lymphatics. Peritoneal reabsorption is continuous and reduces the intraperitoneal volume throughout the dwell (Mactier *et al*., 1987).

The urea clearance is normalized to total body water (volume of urea distribution in the body) and is expressed as Kt/V. The Kt/Vvalue is a number without a unit (mL/min). During intermittent dialysis, with a dialysate flow rate of 30 mL/min, the typical urea clearance is about 18 to 20 mL/min. Increasing the dialysate flow rates to 3.5 to 12 L/h by rapid exchanges increases the urea clearance rate to a maximum of 30 to 40 mL/min. Beyond this maximum rate, the clearance rate begins to decrease owing to the loss of membrane-fluid contact time with infusion and drainage; inadequate mixing may also occur (Penzotti and Mattocks, 1971, Pirpasopoulos *et al*., 1972, Tenckhof *et al*., 1965). Clearance could be enhanced by increasing the membrane-solution contact (Trivedi and Twardowski, 1994). Continuous dialysate flow techniques using either two catheters or double-lumen catheters also have enhanced the urea clearance rate to a maximum of 40 mL/min. At these high flow rates, poor mixing, channeling, abdominal pain, and poor drainage limit successful application. Maintaining a fluid reservoir in the peritoneal cavity (called tidal peritoneal dialysis) and then replacing only a fraction of the intraperitoneal volume rapidly, increases clearance rates by about 30% compared with the standard technique using the same doses owing to maintaining fluid-membrane contact at higher dialysis-solution flow rates (Di Paolo, 1978, Finkelstein and Kliger, 1979, Twardowski *et al*., 1990).

The mass-transfer area coefficient (MTAC)

The MTAC represents the clearance rate by diffusion in the absence of ultrafiltration and when the solute accumulation in the dialysis solution is zero (Randerson, 1980). MTAC is equal to the product of peritoneal membrane permeability (P) and effective peritoneal membrane surface area (S) (Pyle, 1981). Thus, when both capillary blood and dialysate flows are infinite, the clearance rate is directly proportional to the effective peritoneal surface area and inversely proportional to the overall membrane resistance. However, infinite blood and dialysate flows cannot be achieved, and the maximum clearance rate is unattainable. The closest measurable value, the MTAC, was introduced. The MTAC represents an instantaneous clearance without being influenced by ultrafiltration and solute accumulation in the dialysate (Farrell and Randerson, 1980). The MTAC is measured over a test exchange during which at least two blood and dialysate samples are obtained at different dwell times (Pyle *et al*., 1981). The precision of the measurement is enhanced with more data points. The MTAC is seldom used clinically; however, it is a very useful research tool (Garred *et al*., 1983).

Indications

The major indication for peritoneal dialysis is renal failure with oliguria or anuria. It may be indicated if the blood urea nitrogen (BUN) concentration is greater than 100 mg/dL (35 mmol/L) or the serum creatinine concentration is greater than 10 mg/dL (884 umol/L) and medical management has failed to elicit a positive response (Lew *et al*., 2005).

It has also been used for accelerated elimination of certain dialyzable toxins, e.g., ethylene glycol, ethanol, barbiturate overdose, sodium monofluoro-acetate poisoning and to correct severe hyperkalemia, metabolic acidosis, hypercalcemia and hypothermia or hyperthermia (Labato, 2000).

Procedure

Catheter placement is performed using strict aseptic technique and, if possible, in a surgery suite. A urinary catheter should always be placed prior to placement of a dialysis catheter to prevent bladder trauma on insertion (Struijk *et al*., 1994). As catheters are generally placed in animals with acute renal failure, these animals are generally depressed and regardless of technique for catheter placement (percutaneous or minisurgical approach), mild sedation and local anesthesia are frequently sufficient. With the patient in lateral or dorsal recumbency the abdomen is clipped from the xiphoid to the pubis and surgically prepared. Administration of a prophylactic dose of a first generation cephalosporin is recommended prior to catheter insertion (Boen, 1961).

Catheters can be placed via mini surgical

approach, laparoscopically, or percutaneously. No method has proven to be more advantageous. Regardless of the technique used, a subcutaneous tunnel is recommended. The catheter can enter the abdomen on midline or via a paramedian approach, at the level of the umbilicus. The catheter should be directed caudally and positioned in the lower pelvis. Catheter placement should be verified by infusing, and easily retrieving, a small volume of dialysate (2–5 ml) before the catheter is secured (Ash, 2003 and Cowgill, 1995).

Patient parameters are monitored daily includes : (a) perfusion and hydration viz. PCV/TP, blood pressure, heart rate, urine output, temperature, CVP; (b) Electrolytes, BUN, and creatinine; (c) Respiration (respiratory distress can occur from over distention of the abdomen or leakage of dialysate into the pleural cavity); (d) Cytology on effluent dialysate (to monitor for peritonitis).

Complication

Inherent complications associated with peritoneal dialysis include peritoneal access, dialysate leak, inadequate dialysis, hypoalbuminemia, electrolyte abnormalities, pelvic limb edema, catheter exit-site infections, and peritonitis. Peritoneal dialysis may not provide adequate solute removal, especially in larger patients and in patients with declining residual renal function. PD is ultimately limited by the surface area and permeability characteristics of the peritoneal membrane as well as the volume it can contain (Locatelli *et al*., 2005).

Use in managing leptospirosis

A retrospective study of five dogs managed with peritoneal dialysis for ARF caused by leptospirosis was performed by (Beckel *et al*., 2005). All dogs had positive titers for *Leptospira bratislava* (range 1:400–1:6400) and were treated with IV fluids and ampicillin prior to peritoneal dialysis. Median age at presentation was 5 years (range 2–6 years). Median duration of peritoneal dialysis was 4 days (range 3–16 days). Azotemia decreased in all dogs during peritoneal dialysis. At the start of peritoneal dialysis, median BUN was 192 mg/dl (range 140–235) and median creatinine was 12.8 mg/dl (range 7.7–16.9). On the last day of peritoneal dialysis, median BUN was 63 mg/dl and creatinine was 3.4 mg/dl. The most common complications during peritoneal dialysis were hypokalemia (60%), hypoalbuminemia (40%), pelvic limb edema (40%) and CNS signs (40%). Peritonitis was not identified in any of the dogs. Four dogs (80%) survived to discharge from the hospital. Survival in this study was similar to other studies of ARF secondary to leptospirosis with reported survival rates of 82% (18/22) in dogs treated conservatively with antibiotics and IV fluids, and 86% (12/14) in dogs treated with hemodialysis by Lichtenberger (2007).

Conclusion

Peritoneal dialysis is the process of utilizing the peritoneum as a semipermeable membrane in order to move solutes and water between blood in the peritoneal capillaries and ?uid (dialysate) instilled into the peritoneal cavity. Peritoneal dialysis is used most frequently in management of acute kidney injury refractory to ?uid therapy, but it also has been used in management of severe metabolic disturbances, acute poisoning with dialyzable substances (e.g. ethylene glycol, ethanol, barbiturates) and severe temperature extremes.

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